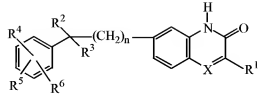
Listing of Claims:

This listing of claims replaces all prior versions, and listings, of claims in the captioned application.

1. (Original) A compound of formula (I),



(I)

the *N*-oxide forms, the addition salts and the stereo-chemically isomeric forms thereof, wherein

n is 0, 1 or 2;

X is N or CR^7, wherein R^7 is hydrogen or taken together with R^1 may form a bivalent radical of formula -CH=CH-CH=CH-;

R^1 is C_{1-6}alkyl or thienyl;

R^2 is hydrogen, hydroxy, C_{1-6}alkyl, C_{3-6}alkynyl or taken together with R^3 may form =O;

R^3 is a radical selected from

-$(CH_2)_s$- NR^8R^9 (a-1),
-O-H (a-2),
-O-R^{10} (a-3),
-S- R^{11} (a-4), or
—C≡N (a-5),

wherein
s is 0, 1, 2 or 3;
R^8 is –CHO, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{1-6}alkylcarbonyl, di(C_{1-6}alkyl)aminoC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkyl, C_{1-6}alkylcarbonylaminoC_{1-6}alkyl, piperidinylC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, C_{1-6}alkyloxy, thienylC_{1-6}alkyl, pyrrolylC_{1-6}alkyl, arylC_{1-6}alkylpiperidinyl, arylcarbonylC_{1-6}alkyl, arylcarbonylpiperidinylC_{1-6}alkyl, haloindozolylpiperidinylC_{1-6}alkyl, or arylC_{1-6}alkyl(C_{1-6}alkyl)aminoC_{1-6}alkyl;

R^9 is hydrogen or C_{1-6}alkyl;

R^{10} is C_{1-6}alkyl, C_{1-6}alkylcarbonyl or di(C_{1-6}alkyl)aminoC_{1-6}alkyl; and

R^{11} is di(C_{1-6}alkyl)aminoC_{1-6}alkyl;

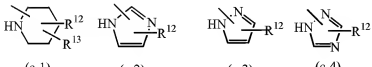
or R^3 is a group of formula

$$-(CH_2)_t\text{-}Z- \qquad \text{(b-1)},$$

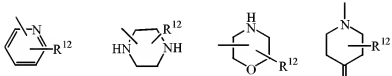
wherein

t is 0, 1, 2 or 3;

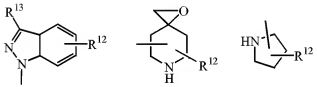
Z is a heterocyclic ring system selected from



(c-1) (c-2) (c-3) (c-4)

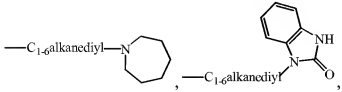


(c-5) (c-6) (c-7) (c-8)



(c-9) (c-10) (c-11)

wherein each R^{12} independently is hydrogen, C_{1-6}alkyl, aminocarbonyl, hydroxy,



C_{1-6}alkyloxyC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkylamino, di(phenylC_{2-6}alkenyl), piperidinylC_{1-6}alkyl, C_{3-10}cycloalkyl, C_{3-10}cycloalkylC_{1-6}alkyl, aryloxy(hydroxy)C_{1-6}alkyl, haloindazolyl, arylC_{1-6}alkyl, arylC_{2-6}alkenyl, morpholino, C_{1-6}alkylimidazolyl, or pyridinylC_{1-6}alkylamino; and

each R^{13} independently is hydrogen, piperidinyl or aryl;

R^4, R^5 and R^6 are each independently selected from hydrogen, halo, trihalomethyl, trihalomethoxy, C_{1-6}alkyl, C_{1-6}alkyloxy, di(C_{1-6}alkyl)amino, di(C_{1-6}alkyl)aminoC_{1-6}alkyloxy or C_{1-6}alkyloxycarbonyl; or

when R^5 and R^6 are on adjacent positions they may taken together form a bivalent radical of formula

-O-CH_2-O (d-1),
-O-$(CH_2)_2$-O- (d-2),
-CH=CH-CH=CH- (d-3), or
-NH-C(O)-NR^{14}=CH- (d-4),
wherein R^{14} is C_{1-6}alkyl;

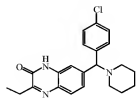
aryl is phenyl or phenyl substituted with halo, C_{1-6}alkyl or C_{1-6}alkyloxy;

with the proviso that when
n is 0, X is N, R^1 is C_{1-6}alkyl, R^2 is hydrogen, R^3 is a group of formula (b-1), t is 0, Z is the heterocyclic ring system (c-2) wherein said heterocyclic ring system Z is attached to the rest of the molecule with a nitrogen atom, and R^{12} is hydrogen; then
at least one of the substituents R^4, R^5 or R^6 is other than hydrogen, halo, C_{1-6}alkyl or C_{1-6}alkyloxy.

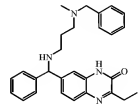
2. (Original) A compound as claimed in claim 1 wherein
n is 0 or 1; X is N or CR^7, wherein R^7 is hydrogen; R^1 is C_{1-6}alkyl; R^2 is hydrogen; R^3 is a radical selected from (a-1) or (a-2) or is group of formula (b-1); s is 0, 1 or 2; R^8 is C_{1-6}alkyl or arylC_{1-6}alkyl(C_{1-6}alkyl)aminoC_{1-6}alkyl; t is 0, 1 or 2; Z is a heterocyclic ring system selected from (c-1), (c-2), (c-3), (c-4), (c-5) or (c-11); each R^{12} independently is hydrogen or C_{1-6}alkyloxyC_{1-6}alkylamino; each R^{13} independently is hydrogen; and R^4, R^5 and R^6 are each independently selected from hydrogen, halo or C_{1-6}alkyl.

3. (Previously Presented) A compound according to claim 1 wherein
n is 0 or 1; X is N; R^1 is C_{1-6}alkyl; R^2 is hydrogen; R^3 is a radical of formula (a-1) or is a group of formula (b-1); s is 0; R^8 is arylC_{1-6}alkyl(C_{1-6}alkyl)aminoC_{1-6}alkyl;
t is 0; Z is a heterocyclic ring system selected from (c-1) or (c-2); each R^{12} independently is hydrogen or C_{1-6}alkyloxyC_{1-6}alkylamino; each R^{13} independently is hydrogen; and R^4, R^5 and R^6 are each independently selected from hydrogen or halo.

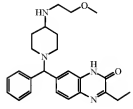
4. (Currently Amended) A compound selected from compound No 5, compound No 9, compound No 2 and compound No 1:



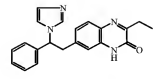
compound 5;



compound 9
$.C_2H_2O_4$ (1:2) ;



compound 2
$.C_2H_2O_4$ (2:5) ; and



compound 1 .

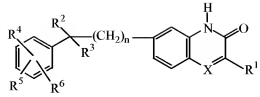
and the *N*-oxide forms, the addition salts and the stereo-chemically isomeric forms thereof.

5. (Cancelled)

6. (Previously Presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient a therapeutically effective amount of a compound according to claim 1.

7. (Cancelled)

8. (Currently Amended) A method of treating in a subject a PARP mediated disorder, said method comprising administering to the subject a therapeutically effective amount of a compound of formula (I)



(I)

the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereo-chemically isomeric forms thereof, wherein

n is 0, 1 or 2;

X is N or CR^7, wherein R^7 is hydrogen or taken together with R^1 may form a bivalent radical of formula -CH=CH-CH=CH-;

R^1 is C_{1-6}alkyl or thienyl;

R^2 is hydrogen, hydroxy, C_{1-6}alkyl, C_{3-6}alkynyl or taken together with R^3 may form =O;

R^3 is a radical selected from

-$(CH_2)_s$- NR^8R^9 (a-1),
-O-H (a-2),
-O-R^{10} (a-3),
-S- R^{11} (a-4), or
—C≡N (a-5),

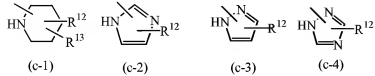
wherein
s is 0, 1, 2 or 3;
R^8 is –CHO, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{1-6}alkylcarbonyl, di(C_{1-6}alkyl)aminoC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkyl, C_{1-6}alkylcarbonylaminoC_{1-6}alkyl, piperidinylC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, C_{1-6}alkyloxy, thienylC_{1-6}alkyl, pyrrolylC_{1-6}alkyl, arylC_{1-6}alkylpiperidinyl, arylcarbonylC_{1-6}alkyl, arylcarbonylpiperidinylC_{1-6}alkyl, haloindozolylpiperidinylC_{1-6}alkyl, or arylC_{1-6}alkyl(C_{1-6}alkyl)aminoC_{1-6}alkyl;
R^9 is hydrogen or C_{1-6}alkyl;
R^{10} is C_{1-6}alkyl, C_{1-6}alkylcarbonyl or di(C_{1-6}alkyl)aminoC_{1-6}alkyl; and
R^{11} is di(C_{1-6}alkyl)aminoC_{1-6}alkyl;
or R^3 is a group of formula

$-(CH_2)_t-Z-$ (b-1),

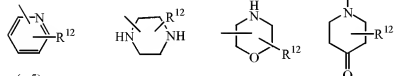
wherein

t is 0, 1, 2 or 3;

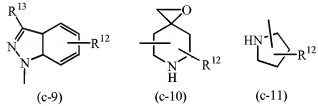
Z is a heterocyclic ring system selected from



(c-1) (c-2) (c-3) (c-4)

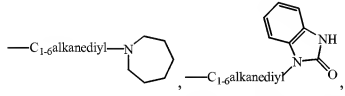


(c-5) (c-6) (c-7) (c-8)



(c-9) (c-10) (c-11)

wherein each R^{12} independently is hydrogen, C_{1-6}alkyl, aminocarbonyl, hydroxy,



C_{1-6}alkyloxyC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkylamino, di(phenylC_{2-6}alkenyl), piperidinylC_{1-6}alkyl, C_{3-10}cycloalkyl, C_{3-10}cycloalkylC_{1-6}alkyl, aryloxy(hydroxy)C_{1-6}alkyl, haloindazolyl, arylC_{1-6}alkyl, arylC_{2-6}alkenyl, morpholino, C_{1-6}alkylimidazolyl, or pyridinylC_{1-6}alkylamino; and

each R^{13} independently is hydrogen, piperidinyl or aryl;

R^4, R^5 and R^6 are each independently selected from hydrogen, halo, trihalomethyl, trihalomethoxy, C_{1-6}alkyl, C_{1-6}alkyloxy, di(C_{1-6}alkyl)amino, di(C_{1-6}alkyl)aminoC_{1-6}alkyloxy or C_{1-6}alkyloxycarbonyl; or

when R^5 and R^6 are on adjacent positions they may taken together form a bivalent radical of formula

-O-CH_2-O (d-1),
-O-$(CH_2)_2$-O- (d-2),
-CH=CH-CH=CH- (d-3), or
-NH-C(O)-NR^{14}=CH- (d-4),
wherein R^{14} is C_{1-6}alkyl;

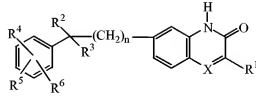
aryl is phenyl or phenyl substituted with halo, C_{1-6}alkyl or C_{1-6}alkyloxy.

9. (Cancelled)

10. (Previously Presented) A method for enhancing the effectiveness of chemotherapy of comprising administration of a compound according to claim 1, in a therapeutically effective amount so as to increase sensitivity of cells to chemotherapy, prior to administration of said chemotherapy .

11. (Previously Presented) A method for enhancing the effectiveness of radiotherapy of comprising administration of a compound accordning to claim 1, in a therapeutically effective amount so as to increase sensitivity of cells to ionizing radiation, prior to administration of said radiotherapy .

12. (Original) A combination of a compound of formula (I) with a chemotherapeutic agent


(I)

the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereo-chemically isomeric forms thereof, wherein

n is 0, 1 or 2;

X is N or CR^7, wherein R^7 is hydrogen or taken together with R^1 may form a bivalent radical of formula -CH=CH-CH=CH-;

R^1 is C_{1-6}alkyl or thienyl;

R^2 is hydrogen, hydroxy, C_{1-6}alkyl, C_{3-6}alkynyl or taken together with R^3 may form =O;

R^3 is a radical selected from

$-(CH_2)_s-NR^8R^9$ (a-1),
-O-H (a-2),
$-O-R^{10}$ (a-3),
$-S-R^{11}$ (a-4), or
$-C\equiv N$ (a-5),

wherein

s is 0, 1, 2 or 3;

R^8, R^{10} and R^{11} are each independently selected from –CHO, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{1-6}alkylcarbonyl, amino, C_{1-6}alkylamino, di(C_{1-6}alkyl)aminoC_{1-6}alkyl, C_{1-6}alkyloxycarbonyl, C_{1-6}alkylcarbonylaminoC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, piperidinyl, piperidinylC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, C_{1-6}alkyloxy, thienylC_{1-6}alkyl, pyrrolylC_{1-6}alkyl, arylC_{1-6}alkylpiperidinyl, arylcarbonylC_{1-6}alkyl, arylcarbonylpiperidinylC_{1-6}alkyl, haloindozolylpiperidinylC_{1-6}alkyl, or arylC_{1-6}alkyl(C_{1-6}alkyl)aminoC_{1-6}alkyl; and

R^9 is hydrogen or C_{1-6}alkyl;

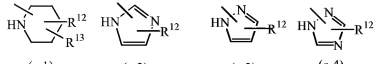
or R^3 is a group of formula

$-(CH_2)_t-Z-$ (b-1),

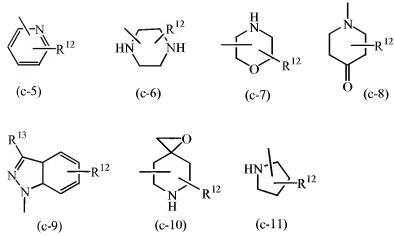
wherein

t is 0, 1, 2 or 3;

Z is a heterocyclic ring system selected from



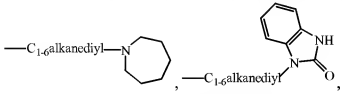
(c-1) (c-2) (c-3) (c-4)



(c-5) (c-6) (c-7) (c-8)

(c-9) (c-10) (c-11)

wherein each R^{12} independently is hydrogen, halo, C_{1-6}alkyl, aminocarbonyl, amino, hydroxy,



aryl, , ,

C_{1-6}alkylaminoC_{1-6}alkyloxy, C_{1-6}alkyloxyC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkylamino, arylC_{1-6}alkyl, di(phenylC_{2-6}alkenyl), piperidinyl, piperidinylC_{1-6}alkyl, C_{3-10}cycloalkyl, C_{3-10}cycloalkylC_{1-6}alkyl, aryloxy(hydroxy)C_{1-6}alkyl, haloindazolyl, arylC_{1-6}alkyl, arylC_{2-6}alkenyl, arylC_{1-6}alkylamino, morpholino, C_{1-6}alkylimidazolyl, or pyridinylC_{1-6}alkylamino;

each R^{13} independently is hydrogen, piperidinyl or aryl;

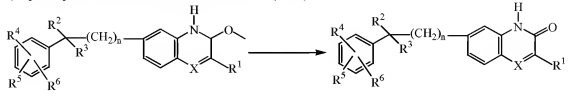
R^4, R^5 and R^6 are each independently selected from hydrogen, halo, trihalomethyl, trihalomethoxy, C_{1-6}alkyl, C_{1-6}alkyloxy, amino, aminoC_{1-6}alkyl, di(C_{1-6}alkyl)amino, di(C_{1-6}alkyl)aminoC_{1-6}alkyloxy or C_{1-6}alkyloxycarbonyl, or C_{1-6}alkyl substituted with 1, 2 or 3 substituents independently selected from hydroxy, C_{1-6}alkyloxy, or aminoC_{1-6}alkyloxy; or when R^5 and R^6 are on adjacent positions they may taken together form a bivalent radical of formula

-O-CH_2-O (d-1),
-O-$(CH_2)_2$-O- (d-2),
-CH=CH-CH=CH- (d-3), or
-NH-C(O)-NR^{14}=CH- (d-4),
wherein R^{14} is C_{1-6}alkyl;

aryl is phenyl or phenyl substituted with halo, C_{1-6}alkyl or C_{1-6}alkyloxy.

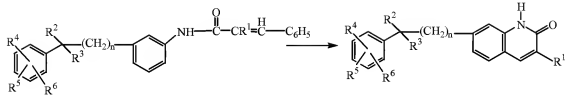
13. (Previously Presented) A process for preparation of a compound as claimed in claim 1, comprising

a) hydrolysis of intermediates of formula (VIII),



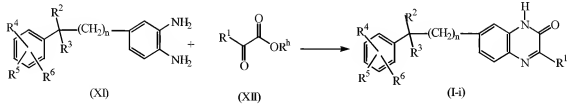
(VIII) (I)

b) cyclization of intermediates of formula (X), into compounds of formula (I) wherein X is CH, herein referred to as compounds of formula (I-j) , and s.



(X) (I-j)

c) condensation of an appropriate ortho-benzenediamine of formula (XI) with an ester of formula (XII) wherein R^h is C_{1-6}alkyl, into compounds of formula (I), wherein X is N, herein referred to as compounds of formula (I-i), in the presence of a carboxylic acid.



(XI) (XII) (I-i)

14. (New) A pharmaceutical composition comprising pharmaceutically acceptable carriers and as an active ingredient a therapeutically effective amount of a compound as claimed in claim 2.

15. (New) A pharmaceutical composition comprising pharmaceutically acceptable carriers and as an active ingredient a therapeutically effective amount of a compound as claimed in claim 3.

16 (New) A pharmaceutical composition comprising pharmaceutically acceptable carriers and as an active ingredient a therapeutically effective amount of a compound as claimed in claim 4.

17. (New) A method of treating in a subject a PARP mediated disorder, said method comprising administering to the subject a therapeutically effective amount of a compound of claim 2.

18. (New) A method for enhancing the effectiveness of chemotherapy comprising administration of a compound according to claim 2, in a therapeutically effective amount so as to increase sensitivity of cells to chemotherapy, prior to administration of said chemotherapy .

19. (New) A method for enhancing the effectiveness of radiotherapy comprising administration of a compound accordning to claim 2, in a therapeutically effective amount so as to increase sensitivity of cells to ionizing radiation, prior to administration of said radiotherapy.

20. (New) A method of treating in a subject a PARP mediated disorder, said method comprising administering to the subject a therapeutically effective amount of a compound of claim 3.

21. (New) A method for enhancing the effectiveness of chemotherapy comprising administration of a compound according to claim 3, in a therapeutically effective amount so as to increase sensitivity of cells to chemotherapy, prior to administration of said chemotherapy .

22. (New) A method for enhancing the effectiveness of radiotherapy comprising administration of a compound accordning to claim 3, in a therapeutically effective amount so as to increase sensitivity of cells to ionizing radiation, prior to administration of said radiotherapy.

23. (New) A method of treating in a subject a PARP mediated disorder, said method comprising administering to the subject a therapeutically effective amount of a compound of claim 4.

24. (New) A method for enhancing the effectiveness of chemotherapy comprising administration of a compound according to claim 4, in a therapeutically effective amount so as to increase sensitivity of cells to chemotherapy, prior to administration of said chemotherapy .

25. (New) A method for enhancing the effectiveness of radiotherapy comprising administration of a compound accordning to claim 4, in a therapeutically effective amount so as to increase sensitivity of cells to ionizing radiation, prior to administration of said radiotherapy.

26 (New) A combination of a compound with a chemotherapeutic agent wherein said compound is a compound of claim 2.

27 (New) A combination of a compound with a chemotherapeutic agent wherein said compound is a compound of claim 3.

28 (New) A combination of a compound with a chemotherapeutic agent wherein said compound is a compound of claim 4.

29. (New) A product made by the process of claim 13.

30. (New) A pharmaceutical composition made by the process of claim 13.